Title	Experimental Studies on the Significance of Pathologic Change in Retroperitoneum at Acute Pancreatitis
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Citation	日本外科宝函 (1966), 35(4): 659-678
Issue Date	1966-07-01
URL	http://hdl.handle.net/2433/207320
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

Experimental Studies on the Significance of Pathologic Change in Retroperitoneum at Acute Pancreatitis

by

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Received for Publication May 12, 1966

CONTENT

I. INTRODUCTION

In producing acute pancreatitis in dogs by injecting autogenous bile into the pancreatic duct, it was recognized that even in cases which showed typical picture of hemorrhagic or necrotic changes, the dogs seldom developed symptoms of shock, showing an unexpectedly fine condition. Different from the human pancreas, the pancreas of dogs exists in the abdominal cavity without being fixed to the retroperitoneum. When the

retroperitoneum was incised and the pancreas was fixed by suture to the margin of the incised retroperitoneum, the animals died within a few hours showing serious symptoms of pancreatitis produced by the method above mentioned. Concerning the cause of death in acute pancreatitis, there have been various assertions, and there is not yet established a radical therapeutic measure for lethal cases dying with fulminant symptoms of shock. HOWARD and JORDAN[1], and SILER and WULSIN[2] described cases of acute pancreatitis died of fulminant development of the disease being accompanied by edema and hemorrhage in the retroperitoneum, despite powerful treatment for shock, and they could not clarify the cause of death in these cases. On the other hand, as the decompressive nerves, the sinus nerve[3][4] distributing in the carotid sinus, the aortic nerve[5] terminating in the aortic arch and other nerves distributing in the auricle[5] and respiratory tract[6] are described, and Stöhr discovered a number of sensory endings in the connective tissue around the abdominal aorta behind the pancreas and he insisted that most of them are VATER PACINI corpuscle and participate in regulation of blood pressure[7][5]. Comparing acute pancreatitis with acute abdominal aortitis, BERNARD[8] maintained that influence of both of these on circulatory system, particularly in development to shock, resembles not a little each other. Human pancreas is a retroperitoneal organ being closely located to the abdominal aorta, and it is readily presumed that pancreatic exudate or its destructive products naturally drains and infiltrates into the retroperitoneum. In this respect, it was recognized that symptoms of acute pancreatitis could be intensified when it was produced in dogs whose pancreas was fixed to the retroperitoneum by suture in order to make anatomical situation of this organ resemble that of human beings. From these observations it was assumed that mechanism of shock development at acute pancreatitis exists in the retroperitoneal organs, particularly in the surroundings of the abdominal aorta. The present experiment was carried out to investigate these problems.

II. MATERIALS AND METHODS

1. Production of Pancreatitis in Dogs

Adult mongrel dogs weighing approximately 10 kg were anesthetized with intravenous injection of isozol of 12 to 15 mg per kg body weight. The abdomen was opened with upper median incision and the accessory pancreatic duct was ligated. Autogenous bile was injected as gently as possible almost without pressure into the main pancreatic duct[9], which was then doubly ligated and the abdomen was closed.

2. Fixation of Pancreas to Retroperitoneum (Fig. 1)

The superior border of the pancreatic head was isolated as carefully as possible. The retroperitoneum was incised in the area of beginning of the superior mesenteric artery, i. e. in the area of celiac ganglion, carefully preventing eventual injury. Previously isolated superior border of the pancreatic head was tightly sutured to the margin of the incised retroperitoneum.

3. Measurement of Arterial and Portal Pressures

The femoral artery was exposed and a canula was inserted, which was connected to an U shaped mercurial manometer for measurement of arterial pressure. Portal pressure was measured by an aqueous manometer connected to a vinyl tube inserted into the portal

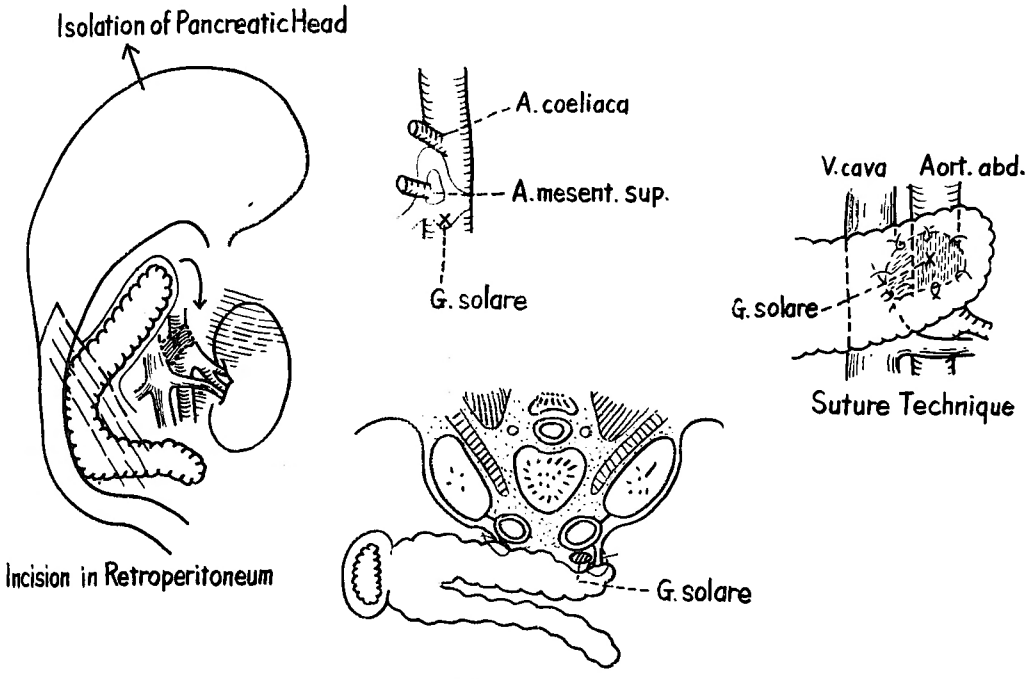

Fig. 1 Fixation of Pancreas to Retroperitoneum

vein through an exposed branch of the mesenteric vein.

4. Determination of Portal Blood Flow

The portal vein was exposed and portal blood flow was determined by the use of electromagnetic flow meter devised by Hori, in our clinic.

5. Staining of Nerves

Nervous tissue around the abdominal aorta was stained following silver impregnating method of BIELSCHOWSKY and SUZUKI[10)11)], and myelin sheath staining of SUGAMO[12)].

III. RESULTS

1. Influence of Fixation of Pancreas to Retroperitoneum on Production of Acute Pancreatitis

   i. Dogs of Acute Pancreatitis without Fixation of Pancreas to Retroperitoneum (Tab. 1)

Table 1 Injection of Bile of 0.2cc/kg Bodyweight without Fixation of the Pancreas.

Dog No.	Survival Time (Day)
16	7 (Slaughter)
17	7 (Slaughter)
14	7 (Slaughter)
13	7 (Slaughter)
5	7 (Slaughter)

Acute pancreatitis was produced by the method of autogenous bile injection, as described in the above. Autogenous bile of 0.2 cc/kg body weight was injected into the pancreatic duct almost without pressure. All 5 animals survived and they were slaughtered on 7th day.

   ii. Experiment of Fixation of Pancreas in Dogs without Pancreatitis (Tab. 2)

Table 2 Survival Time of Dog with Fixation of the Pancreas.

Dog No.	Survival Time (Day)
1	7 (Slaughter)
2	7 (Slaughter)
4	7 (Slaughter)
7	7 (Slaughter)

Table 3 Survival Time of Dog with Fixation of the Pancreas and acute Pancreatitis.

Dog No.	Survival Time (Hours)
3	5
21	6
22	12
20	14
12	17
18	19
6	19
25	21
28	24

When the pancreas was fixed to the retroperitoneum with simultaneous ligation of the main and accessory pancreatic ducts, all 4 animals survived for 7 days.

iii. Dogs of Acute Pancreatitis with Fixation of Pancreas to Retroperitoneum (Tab. 3)

When the pancreas was fixed to the retroperitoneum and autogenous bile of 0.2 cc/kg body weight was injected into the pancreatic duct, all 9 animals died from 5 to 24 hours after the injection.

2. Influence of Fixation of Pancreas to Retroperitoneum on Arterial and Portal Pressures

Arterial and portal pressures were measured in dogs of acute pancreatitis produced by autogenous bile of 0.4 cc/kg body weight with and without Fixation of the pancreas to the retroperitoneum.

i. Dogs of Acute Pancreatitis without Fixation of Pancreas to Retroperitoneum (Tab. 4, Fig. 2)

Simultaneously with the injection of autogenous bile, arterial pressure began to decrease from normal level of 110 mmHg to 98 mmHg within 10 minutes, showing no marked

Table 4 Arterial and Portal Pressures in Dogs of acute Pancreatitis without Fixation of the Pancreas. (Bile Injection of 0.4 cc/kg Bodyweight)

	Arterial Presture (mmHg)						Portal Pressure (mmH_2O)					
Time after Injection (Min.)	No. 9	No. 10	No. 11	No. 15	No. 32	mean	No. 9	No. 10	No. 11	No. 15	No. 32	mean
Before	115	114	107	105	109	110	115	120	103	100	112	110
5	109	106	99	97	94	102	98	107	94	91	110	100
10	104	102	96	94	94	98	110	101	100	95	119	105
20	102	96	95	93	99	96	130	150	125	115	155	135
30	104	102	97	93	94	99	145	149	139	136	146	143
40	102	99	92	88	79	95	147	148	142	137	145	145
50	90	85	79	77	80	82	146	147	145	135	149	144
60	88	87	78	77	70	82	147	145	143	132	146	141
70	81	78	69	67	69	73	143	145	135	138	149	143
80	76	73	69	68	66	71	140	145	140	135	148	141
90	74	70	66	64	64	68	144	145	137	138	146	142
100	70	68	63	60	68	65	144	145	137	135	149	142
110	74	72	66	65	68	69	148	146	137	134	146	143
120	75	73	68	65	68	70	147	145	139	136	142	141

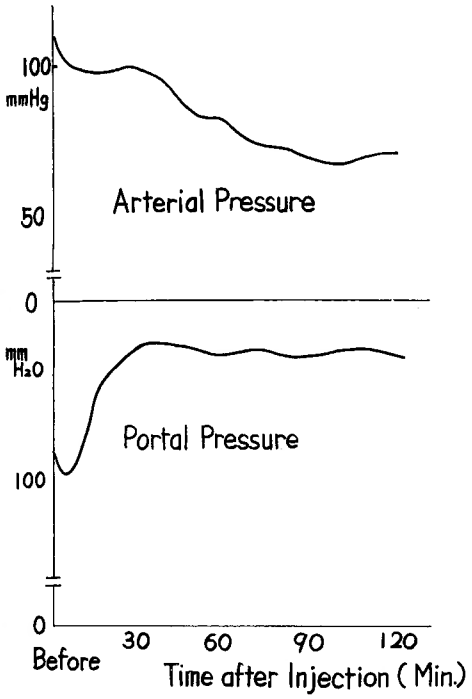

Fig. 2 Arterial and Portal Pressures in Dogs of Acute Pancreatitis without Fixation of the Pancreas (Bile Injection of 0.4 cc/kg Body Weight)

change thereafter until 40 minutes after the injection. Arterial pressure fell to 70mmHg 120 minutes after the injection, showing gradual decrease. Portal pressure decreased from normal level of 110 mmH_2O to 100 mmH_2O within 5 minutes, which was followed by rapid increase reaching 145 mmH_2O 25 minutes after the injection and maintained approximately constant level thereafter.

ii. Dogs with Fixation of Pancreas without Acute Pancreatitis (Tab. 5, Fig. 3)

The superior border of the pancreatic head was fixed with suture to the retroperitoneum and the accessory and main pancreatic ducts were ligated. Arterial and portal pressures were measured in these dogs, the former showing little change from 113 mmHg to 112 mmHg 120 minutes later. Portal pressure also showed little change from 123 mmH_2O to 122 mmH_2O 120 minutes later.

iii. Dogs of Acute Pancreatitis with Fixation of Pancreas to Retro-

Table 5 Arterial and Portal pressures in Dogs with Fixation of the Pancreas (without Pancreatitis)

Time after Fixture (Min.)	Arterial Pressure (mmHg)			Portal Pressure (mmH_2O)		
	No. 8	No. 23	mean	No. 8	No. 23	mean
Before	110	115	113	120	126	123
5	112	114	113	121	129	125
10	113	114	114	122	129	126
20	114	112	113	122	131	126
30	114	112	113	119	129	124
40	114	112	113	118	130	124
50	113	110	112	117	128	123
60	112	110	111	118	129	124
70	109	112	111	120	128	124
80	108	111	110	121	129	126
90	108	113	111	119	130	125
100	111	114	113	115	128	122
110	114	113	114	116	129	123
120	112	112	112	117	126	122

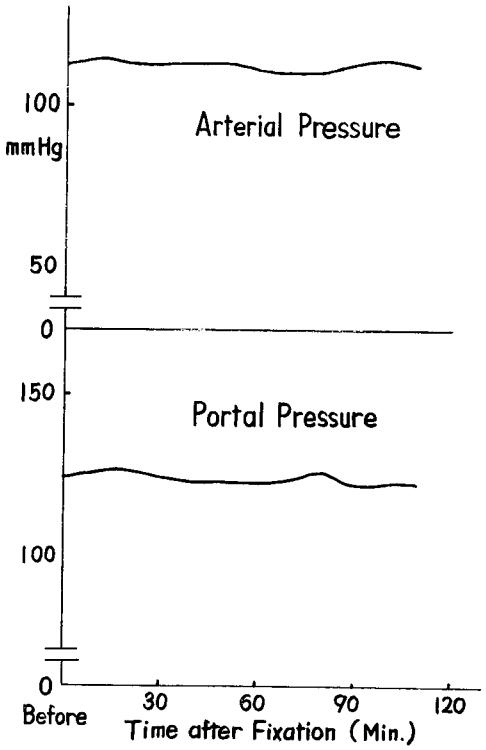

Fig. 3 Arterial and Portal Pressures in Dogs with Fixation of the Pancreas without Acute Pancreatitis.

peritoneum (Tab. 6, Fig. 4)

Simultaneously with injection of autogenous bile, arterial pressure began to decrease rapidl yfrom 105 mmHg to 55 mmHg until 15 minutes after injection, which was followed by gradual decrease with slight fluctuation reaching a level of 50 mmHg 40 minutes after injection and 20 mmHg 120 minutes after injection, and the animals died approximately 150 minutes after injection. Portal pressure of 125 mmH_2O elevated to 140 mmH_2O within 5 minutes, which was followed by gradual fall until ultimate death.

3. Influence of Trypsin Infusion into Retroperitoneum

i. Infusion into Peritoneal Cavity (Tab. 7, Fig. 5)

By infusion of trypsin of 250 mg into the peritoneal cavity, arterial pressure rapidly descended until 30 minutes after the infusion from 115 mmHg to 72 mmHg, reaching 68 mmHg 70 minutes after the infusion and 65 mmHg 120 minutes after the infusion.

Table 6 Arterial and Portal Pressures after Injection of Autogenous Bile into the Pancreatic Duct (0.4 cc/kg Body weight) in Dogs with Fixation of the Pancreas.

	Arterial Pressure (mmHg)							Portal Pressure (mmH_2O)						
Time after Infusion (min.)	No. 33	No. 19	No. 23	No. 26	No. 34	No. 24	Mean	No. 33	No. 19	No. 23	No. 26	No. 34	No. 24	Mean
Before	110	100	115	95	102	108	105	120	120	128	132	130	120	125
5	65	66	76	55	85	73	70	137	138	142	140	140	143	140
10	52	48	64	50	62	66	57	130	134	126	126	127	141	131
15	50	47	65	50	53	65	55	122	129	120	119	121	127	123
20	60	52	60	53	63	66	59	125	128	122	128	125	122	125
25	61	51	62	50	57	61	57	126	122	120	117	125	122	122
30	55	48	58	46	53	52	52	118	115	119	113	115	122	117
35	51	45	50	45	51	41	48	114	110	114	113	111	116	113
40	48	49	48	52	51	52	50	115	113	114	115	113	114	114
45	49	47	48	54	48	54	50	115	114	112	116	114	113	114
50	50	46	48	54	46	55	50	115	115	111	114	115	116	114
55	51	47	51	50	45	56	50	114	117	112	112	115	116	114
60	51	48	52	45	43	49	48	114	116	113	112	115	120	115
65	47	47	51	44	40	47	46	115	111	117	109	110	110	112
70	40	43	43	41	36	37	40	108	108	114	105	108	105	108
75	35	36	36	40	32	31	35	101	102	105	102	105	103	103
80	35	35	36	40	32	32	35	99	99	103	98	105	102	101
85	36	35	35	40	32	32	35	102	102	102	98	104	104	102
90	37	32	37	38	31	35	35	101	102	104	99	105	107	103
95	37	32	38	37	30	35	35	103	103	101	99	104	102	102
100	35	32	35	35	28	33	33	93	96	98	97	96	96	96
105	35	32	34	32	25	33	32	88	92	91	90	93	86	90
110	30	28	29	25	23	27	27	84	88	88	82	87	81	85
115	25	25	25	24	21	24	24	82	84	79	78	86	78	83
120	20	20	22	23	18	17	17	77	79	67	65	82	76	74
Time of Death (Min.)	140	135	170	160	155	130	150							

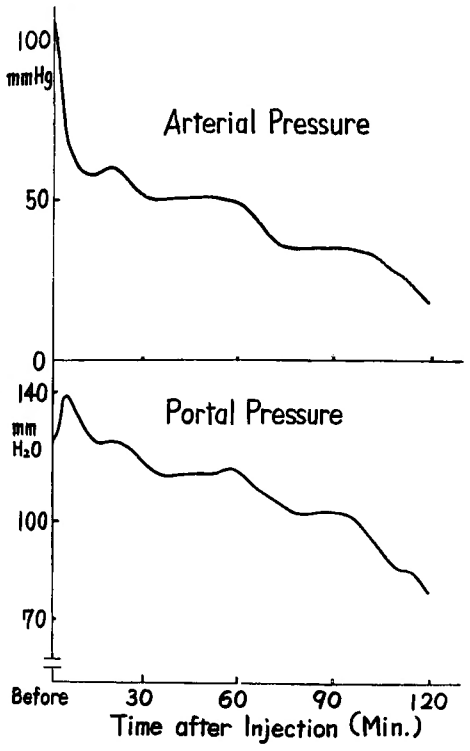

Fig. 4 Arterial and Portal Pressures in Dogs with Fixation of Pancreas and with acute Pancreatitis produced by Injection of Bile of 0.4 cc/kg Body Weight.

Portalpressure of 126 mmH_2O increased to 142 mmH_2O within 5 minutes after infusion of trypsin, which then decreased to 125 mmH_2O 10 minutes after infusion. Portal pressure gradually increased thereafter to 142 mmH_2O 70 minutes after infusion and 149 mmH_2O 120 minutes after infusion.

ii. Infusion into Retroperitoneum (Tab. 8, Fig. 6)

When trypsin of 250 mg was injected into the retroperitoneum around the abdominal aorta in the level of the bifurcation of the superior mesenteric artery, arterial pressure rapidly decreased from 112 mmHg to 36 mmHg 15 minutes after injection, which was followed by gradual fall until ultimate death 90 minutes after injection. Portal pressure decreased from 118 mmH_2O to 88 mmH_2O 70 minutes after injection more gradually compared with decrease in arterial pressure. Portal blood flow was 98 cc per minutes before the injection of trypsin, which rapidly decreased simultaneously with the injection being estimated to be 33 cc per minute 25 minutes after injection and 20 cc per minute 40 minutes after injection. The decrease in portal blood flow became remarkable from 70 minutes after the injection, reaching 4 cc per minute 90 minutes after injection and the animals died. During this observation, portal pressure decreased from 125 mmH_2O to 55 mmH_2O (Tab. 9, Fig. 7).

4. Influence of Incision in Retroperitoneum (Tab. 10, Fig. 8).

i. Dogs of Acute Pancreatitis with Fixation of Pancreas to Retroperitoneum

The superior border of the pancreatic head was fixed with suture to the retroperitoneum. A small incision was laid the retroperitoneum and autogenous bile of 0.4 cc/kg body weight was injected into the pancreatic duct to produce acute pancreatitis. In these animals, arterial and portal pressures were measured. Arterial pressure decreased 120 minutes after the injection of bile from 111 mmHg to 64 mmHg and portal pressure increased within 10 minutes from 121 mmH_2O to 153 mmH_2O and gradually decreased thereafter reaching 113 mmH_2O 60 minutes after the injection. Portal pressure remained in that level until 110 minutes after the injection of bile and again began to decrease reaching 109 mmH_2O 120 minutes after the injection. Average survival time was 325 minutes.

ii. Infusion of Trypsin in Retroperitoneum (Tab. 11, Fig. 9).

A small incision was laid in the retroperitoneum and trypsin of 250 mg was similarly

Table 7 Arterial and Portal Pressures after Infusion of Trypsin of 250mg in Peritoneal Cavity.

Time after Infusion (Min.)	Arterial pressure (mmHg)				Portal Pressure (mmH_2O)			
	No. 45	No. 43	No. 47	mean	No. 45	No. 43	No. 47	mean
Before	110	120	115	115	132	125	121	126
5	103	111	109	108	136	144	145	142
10	95	95	102	97	116	132	126	125
15	87	81	91	87	122	130	125	126
20	80	72	83	78	128	129	125	127
25	72	69	77	73	132	129	126	129
30	73	67	76	72	135	131	127	131
35	74	67	78	73	138	133	129	133
40	72	68	75	72	139	136	132	136
45	70	69	74	71	141	138	135	138
50	68	69	73	70	143	138	137	139
55	67	69	71	69	145	136	139	140
60	66	70	71	69	147	134	140	140
65	65	70	69	68	148	134	141	141
70	64	71	68	68	150	135	141	142
75	64	72	68	68	152	136	142	143
80	63	74	67	68	153	137	143	144
85	62	75	67	68	154	137	143	145
90	62	75	66	68	155	137	143	145
95	62	74	66	67	156	137	144	146
100	61	73	66	67	157	139	144	147
105	61	72	65	66	158	137	144	146
110	60	71	65	65	160	136	146	147
115	60	70	65	65	161	137	148	149
120	60	69	66	65	162	136	148	149

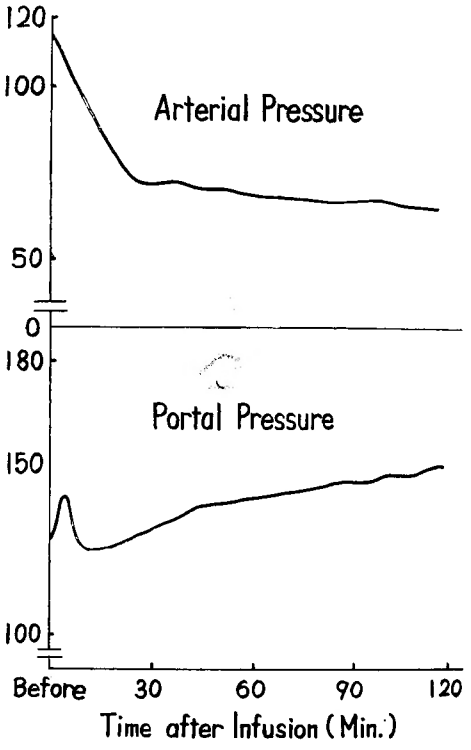

Fig. 5 Arterial and Portal Pressures after Infusion of Trypsin into the Peritoneal Cavity. (Trypsin 250 mg)

injected as in experiment of trypsin injection into the retroperitoneum. Arterial pressure gradually decreased from 119 mmHg to 59 mmHg 70 minutes after the injection of trypsin and it became 53 mmHg 120 minutes after the injection. Portal pressure elevated from 118 mmH_2O to 151 mmH_2O within 20 minutes, which was followed by gradual fall reaching 136 mmH_2O 70 minutes after the injection and 134 mmH_2O 120 minutes after the injection.

5. Staining of Nerves
   i. Dogs of Acute Pancreatitis without Fixation of Pancreas to Retroperitoneum
      a) Ganglion Cells (Photo 1)
         Neither degeneration nor other pathologic change could be observed.
      b) Nerves in Connective Tissue around Abdominal Aorta (Photo 2 and 3)

Table 8 Arterial and Portal Pressures after Infusin of Trypsin of 250mg into Retroperitoneum.

Time after Infusion (min.)	Arterial Pressure (mmHg)					Portal Pressure (mmH_2O)				
	No. 24	No. 36	No. 37	No. 40	mean	No. 24	No. 36	No. 37	No. 40	mean
Before	105	115	120	110	113	116	122	120	114	118
5	63	96	110	85	89	115	119	118	111	115
10	30	70	90	47	59	105	113	117	109	114
15	24	42	45	34	36	104	109	113	108	109
20	21	35	30	32	30	99	106	105	105	104
25	19	31	25	31	27	95	103	101	105	101
30	18	28	23	30	25	94	100	101	104	100
35	17	27	22	29	24	93	96	100	104	98
40	15	26	21	29	23	93	94	99	104	98
45	13	24	20	28	21	94	93	100	104	98
50	12	22	19	27	20	94	92	98	103	97
55	11	21	19	25	19	93	90	97	103	96
60	10	20	18	24	18	90	89	95	102	94
65	7	19	18	22	17	84	87	93	102	92
70	0	17	18	20	15	77	85	90	100	88
Time of Death (min.)	70	95	100	105	93					

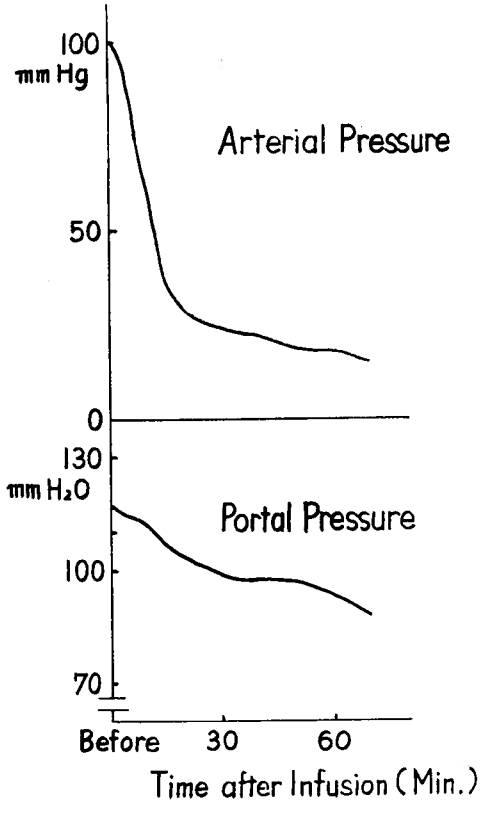

Fig. 6 Arterial and Portal Pressures after Infusion of Trypsin into the Retroperitoneum. (Trypsin 250 mg)

Table 9 Portal Blood Flow after Infusion of Trypsin of 250 mg into Retroperitoneum.

Time after Infusion (min.)	Portal Pressure (mmH_2O)	Portal Blood Flow (cc/min.)
Before	125	98
5	122	
10	118	Determination impossible
15	115	
20	114	
25	114	33
30	114	23
35	113	22
40	110	21
45	105	20
50	99	20
55	93	20
60	89	20
65	86	20
70	82	20
75	78	17
80	75	12
85	67	8
90	55	4

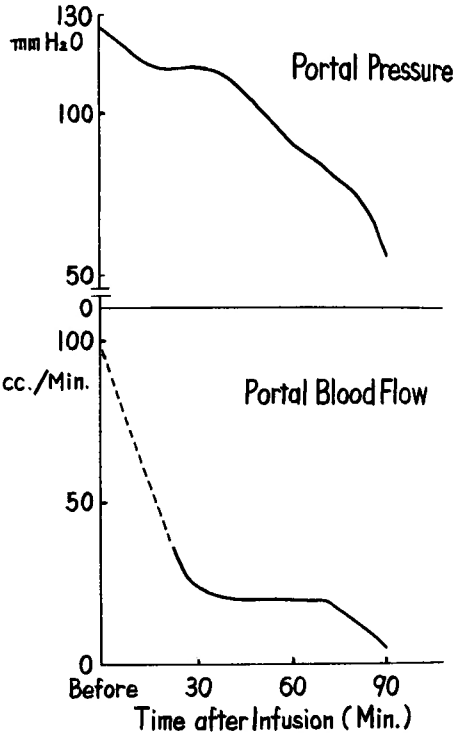

Fig. 7 Portal Blood Flow after Infusion of Trypsin of 250 mg into Retroperitoneum.

Any degenerative and pathologic changes could not be observed.

c) Nerves in Adventitia of Abdominal Aorta (Photo 4 and 5)
Any degenerative and pathologic changes could not be observed.

d) Nerves in Media of Abdominal Aorta (Photo 6)
Any degenerative and pathologic changes could not be observed.

ii. Dogs of Acute Pancreatitis with Fixation of Pancreas to Retroperitonem

a) Ganglion Cells
Transposition of nuclei (Photo 7), Disappearance of nuclei and irregular arrangement of polar cells (Photo 8) could be observed.

b) Nerves in Connective Tissue around Abdominal Aorta
Vacuole formation, irregular swelling (Photo 9), irregular tortuosity (Photo 10), irregular swelling (Photo 11 and 12) and drop-like fragmentation (Photo 13) could be observed.

c) Nerves in Adventitia of Abdominal Aorta
Irregular tortuosity and swelling (Photo 14 and 15) could be observed.

d) Nerves in Media of Abdominal Aorta
Pathologic changes could not be clarified (Photo 16).

Table 10 Arterial and Portal Pressures in Dogs with Fixation of Pancreas and Incision in Retroperitoneum and with acute Pancreatitis Produced by Injection of Bile of 0.4 cc/kg Body weight.

Time after Injection (Min.)	Arterial Pressure (mmHg)					Portal Pressre (mmH_2O)				
	No. 27	No. 35	No. 38	No. 39	mean	No. 27	No. 35	No. 38	No. 39	mean
Before	115	118	110	102	111	120	125	122	117	121
10	100	105	98	93	99	154	159	150	148	153
20	100	103	95	90	97	140	138	133	137	137
30	97	99	92	90	95	138	135	134	137	136
40	92	94	84	92	91	128	130	135	134	132
50	78	84	80	87	82	115	121	124	114	119
60	68	78	74	72	73	110	117	113	113	113
70	65	73	69	67	69	112	116	108	114	113
80	66	71	66	63	67	111	116	106	112	111
90	68	72	65	62	67	112	116	106	109	108
100	69	74	65	62	68	113	116	111	109	112
110	67	73	65	62	67	111	116	106	112	111
120	60	69	65	62	64	105	111	107	113	109
Time of Death (min.)	330	350	320	300	325					

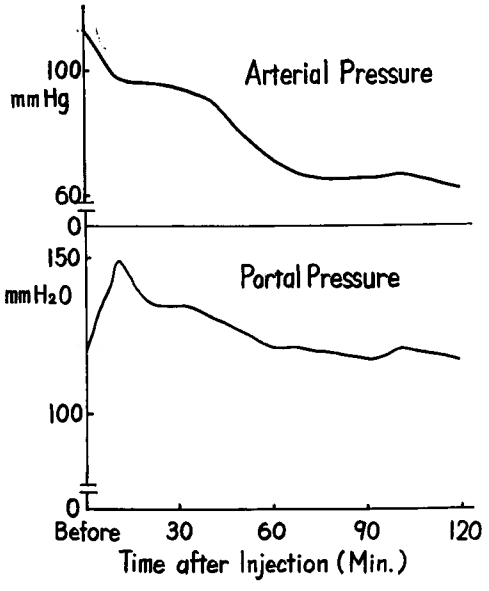

Fig. 8 Arterial and Portal Pressures in Dogs with Fixation of Pancreas and Retroperitoneal Incision and with acute Pancreatitis produced by Injection of Bile of 0.4 cc/kg Body Weight.

Table 11 Arterial and Portal Pressures in Dogs with Retroperitoneal Incision and Infusion of Trypsin into the Retroperitoneum. (Trypsin 250 mg)

Time after Infusion (min.)	Arterial Pressure (mmHg)				Portal Pressure (mmH_2O)			
	No. 46	No. 41	No. 42	mean	No. 46	No. 41	No. 42	mean
Before	120	125	110	119	112	125	116	118
5	103	117	95	105	130	139	131	134
10	94	107	87	96	138	152	142	144
15	88	100	82	90	143	157	149	150
20	84	95	77	85	146	155	152	151
25	79	85	74	79	148	144	153	148
30	76	77	71	75	152	137	149	146
35	73	72	68	71	151	137	142	143
40	69	68	64	67	149	139	138	142
45	65	66	62	64	145	140	135	140
50	62	66	61	63	140	139	135	138
55	58	67	61	62	137	138	136	137
60	58	66	60	61	134	138	138	137
65	56	63	60	60	133	138	139	137
70	56	61	59	59	133	136	138	136
75	54	59	59	57	133	135	139	136
80	54	58	59	57	131	136	139	135
85	53	58	59	57	131	135	138	135
90	53	57	58	56	130	135	140	135
95	53	56	57	55	129	134	140	134
100	53	55	56	55	128	133	139	133
105	52	54	56	54	127	132	138	132
110	52	54	56	54	126	133	139	133
115	51	54	55	53	126	134	141	134
120	51	54	55	53	126	135	141	134

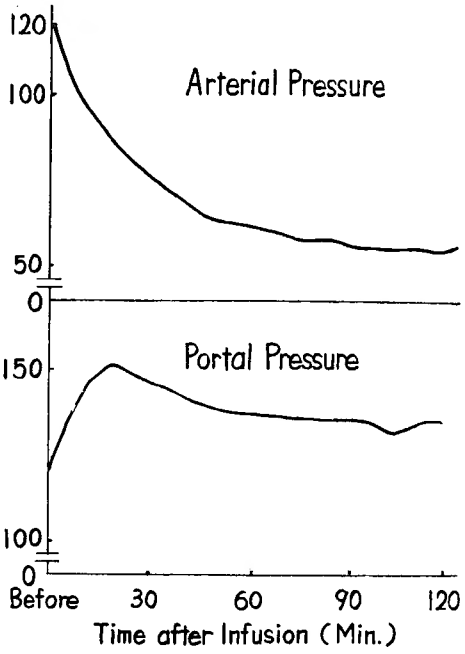

Fig. 9 Arterial and Portal Pressures after Infusion of Trypsin of 250 mg into Retroperitoneum in Dogs with Retroperitoneal Incision.

IV. DISCUSSION

There have been many assertions on the cause of death in acute pancreatitis and it is considered that there is no radical therapeutic measure for cases dying abruptly from fulminant symptoms of shock. HOWARD described dead cases of acute pancreatitis showing fulminant course of the disease being accompanied by edema and hemorrhage in the retroperitoneum, despite powerful antishock treatments, and he reported that the cause of death could not be clarified. In the present experiment, pancreatitis was produced in dogs by injecting autogenous bile into the pancreatic duct. Acute pancreatitis thus produced showed various pictures of the disease depending on the amount and pressure of bile injection into the pancreatic duct, and depending on presence or absence of the ligation of

the accessory pancreatic duct. For instance, when autogenous bile of 0.3 cc/kg body weight was injected as gently as possible almost without pressure and the accessory pancreatic duct was ligated, some animals died within 3 days and others survived, whereas autogenous bile of 0.2 cc/kg body weight resulted in typical acute pancreatitis not followed by shock symptoms and all the animals survived.

Human pancreas is one of the retroperitoneal organs, being largely different from that of dogs which is freely located in the peritoneal cavity. From the presumption that this difference of anatomical situation of the pancreas might participate in the development of shock at acute pancreatitis, some experience was planned to make the pancreas of dogs resemble that of human beings. Namely, the pancreas was fixed with suture to the retroperitoneum in dogs and the main and accessory pancreatic ducts were ligated. Animals all survived suggesting little influence of this operative procedure itself. When the pancreas was fixed to the retroperitoneum in dogs and acute pancreatitis was induced as described in the above, animals all died within 5 to 24 hours, showing inflammatory edema and hemorrhage around the abdominal aorta caused by infiltration of pancreatic juice. The more intense degree of this inflammatory edema and hemorrhage, occured the earlier animals died. Although some other animals showed inflammatory findings in the thoracic cavity, accumulation of intrathoracic fluid, as reported by Good-Pasture[13], could not be observed in any case. Animals also died invariably even when deprived of intense inflammatory findings only with hyperemia and slight accumulation of bloody exudate and also deprived of macroscopic findings of fat necrosis. Then, autogenous bile of 0.4 cc/kg body weight was injected into the pancreatic duct and pancreatitis was produced, and arterial and portal pressures were examined. Arterial pressure of 110 mmHg gradually decreased to 70 mmHg 120 minutes after the injection of bile, and portal pressure of 110 mmH_2O increased to 141 mmH_2O 120 minutes after the injection. No marked change could be observed in arterial and portal pressures when the pancreas was fixed to the retroperitoneum with the ligation of the main and accessory pancreatic ducts, without the injection of bile. When the acute pancreatitis was induced in these dogs with fixation of the pancreas to the retroperitoneum, arterial pressure of 105 mmHg became 20 mmHg 120 minutes after the injection showing more rapid decrease compared with dogs without the fixation of the pancreas. Portal pressure of 125 mmH_2O decreased to 74 mmH_2O 120 minutes after the injection of bile. Animals died 150 minutes after the injection of bile, on the average. It is assumed from these findings that the disease picture could be intensified in dogs of acute pancreatitis with the fixation of the pancreas.

It has been widely accepted that trypsin has an important significance in the disease process of acute pancreatitis among various pancreatic enzymes. When 250 mg of trypsin was infused into the peritoneal cavity, blood pressure fell from 115 mmHg to 65 mmHg 120 minutes after the infusion and portal pressure elevated from 126 mmH_2O to 149 mmH_2O within 120 minutes, excluding initial fluctuation. When trypsin was infused into the retroperitoneum, arterial pressure decreased from 112 mmHg to 36 mmHg 15 minutes after the infusion and animals died about 90 minutes after the infusion. Portal pressure fell from 118 mmH_2O to 88 mmH_2O 70 minutes after the infusion. Portal blood flow rapidly decreased from 98 cc/min. to 4 cc/min. 90 minutes after the infusion of bile and

the animals died about this time. In short, intraperitoneal infusion of trypsin resulted in more gradual decrease in arterial pressure than the infusion into the retroperitoneum and it showed tendency of an increase in portal pressure.

Then, the influence of retroperitoneal incision on acute pancreatitis provoked by the injection of bile together with the fixation of the pancreas to the retroperitoneum and on infusion of trypsin into the retroperitoneum was studied. The pancreas was fixed with suture to the retroperitoneum and an incision was laid in the retroperitoneum. Acute pancreatitis was produced in these animals by injecting autogenous bile of 0.4 cc/kg body weight. Arterial pressure decreased from 115 mmHg to 64 mmHg 120 minutes after the injection of bile and portal pressure became from 120 mmH_2O to 109 mmH_2O 120 minutes after the injection of bile. The animals died 325 minutes after the injection of bile, on the average. Decrease in arterial and portal pressures was more gradual in cases with incision of the retroperitoneum than in those without the incision and survival time was prolonged in the former. From these findings, it is assumed that at acute pancreatitis retroperitoneal incision has an effect on the prolongation of survival time.

When an incision was laid in the retroperitoneum and trypsin was infused into the retroperitoneum, arterial pressure gradually decreased from 119 mmHg to 53 mmHg 120 minutes after the infusion and portal pressure slightly increased from 118 mmH_2O to 134 mmH_2O 120 minutes after the infusion. From these findings, it is considered that infiltration of trypsin into the retroperitoneum was alleviated by the incision of the retroperitoneum and changes in the pressures became more mild than in the occasion of trypsin infusion into the retroperitoneum, which finding being accepted to suggest important influence of trypsin on the retroperitoneal organs.

In the histological findings of the nerves in dogs of acute pancreatitis without fixation of the pancreas to the retroperitoneum, degeneration or pathologic changes could not be observed in the ganglion cells and the nerves in the connective tissue around the abdominal aorta, in the adventitia of the abdominal aorta and in the media of the abdominal aorta. In cases of acute pancreatitis of the dogs whose pancreas was fixed to the retroperitoneum, degeneration was observed in the ganglion cells and the nerves in the connective tissue around the abdominal aorta, and pathologic changes could be found in the nerves in the adventitia of the abdominal aorta, changes in the media of the abdominal aorta being obscure. These findings can be accepted to indicate that pancreatic exudate infiltrated, at acute pancreatitis, to the ganglion cells, surroundings of the abdominal aorta and adventitia of the abdominal aorta. Comparing acute pancreatitis with acute abdominal aortitis, BERNARD pointed out a common feature of readiness particularly to shock state among the symptoms of circulatory system in these two diseases.

Concerning the reflex of blood pressure descension, STÖHR discovered numerous sensory endings of Vater Pacini corpuscle in the connective tissue around the abdominal aorta which passes the retroperitoneum behind the pancreatic body and he postulated that these sensory endings exert regulation of blood pressure. By the way, these corpuscles belong to sensory ending of the splanchnic nerve[14]. MITCHELL[15] also insisted that centripetal fibres are included in the splanchnic nerve and there exist nervous cells around the abdominal aorta. Centripetal fibres in the major and minor splanchnic nerves passes through

the celiac ganglion with centripetal fibres of the smallest splanchnic nerve and enter the sympathetic trunk between 6 th and 12 th sympathetic thoracic ganglion, through which they further enter the corresponding posterior radicles of the spinal cord.[16] On the other hand, SETO[5] asserted that the nervous element around the abdominal aorta might participate in regulation of blood pressure. According to the findings of the present experiment of fixation of the pancreas to the retroperitoneum, infusion of trypsin into the retroperitoneum and staining of the nerves, it is assumed that these nerves largely participate in lowering of blood pressure.

HIRSCH[7] observed that there frequently exist glomerular or capsulated nervous endings in the adventitia of the large arteries, which were considered by STÖHR to participate in regulation of blood pressure. Pathologic changes of the nerves in the adventitia of the abdominal aorta observed in the present experiment are also accepted to exert an influence on the apparatus of the regulation of blood pressure. The nerves in the media of the abdominal aorta was demonstrated to be sensory ones by KIMURA[19] and he also insisted that these nerves participate in the regulation of blood pressure. In the present experiment, however, its role could not be clarified.

V. SUMMARY

Experiments were carried out in order to clarify signficance of pathologic changes in the retroperitoneum at acute pancreatitis produced experimentally in dogs.

1. When acute pancreatitis was produced by injection of autogenous bile of 0.2 cc/kg body weight, all animals survived.

2. The pancreas of dogs is not attached to the retroperitoneum. In order to make dog pancreas resemble that of human beings, the superior border of the pancreatic head was fixed with suture to the retroperitoneum in dogs. All dogs survived this procedure of the fixation revealing little influence of the procedure itself. When the pancreas was fixed to the retroperitoneum and autogenous bile of the same amount was injected to produce acute pancreatitis, all animals died from 5 to 24 hours after injection of the bile, revealing edema and hemorrhage in the retroperitoneum.

3. In dogs of acute pancreatitis produced by injecting autogenous bile of 0.4 cc/kg body weight, blood pressure gradually decreased and portal pressure increased. On the other hand, changes could not be observed merely by the fixation of the pancreas to the retroperitoneum and ligation of the main and accessory pancreatic ducts. When acute pancreatitis was produced in dogs with the fixation of the pancreas to the retroperitoneum, blood pressure decreased abruptly and portal pressure also decreased.

4. When trypsin of 250 mg was infused into the peritoneal cavity, blood pressure gradually decreased and portal pressure showed the tendency of increase. When trypsin was infused into the retroperitoneum, blood pressure decreased abruptly and portal pressure also decreased.

5. In order to clarify the influence of retroperitoneal incision, a small incision was laid in the retroperitoneum and autogenous bile of 0.4 cc/kg body weight was injected into the pancreatic duct in dogs whose pancreas was fixed to the retroperitoneum. Blood and portal pressures in these animals more gradually decreased than in animals without

the incision, survival time also being prolonged in the former. When trypsin of 250 mg was infused in the retroperitoneum after small incision was laid in the retroperitoneum, arterial pressure decreased more gradually than that in animals without the incision and portal pressure increased.

6. From the studies on the nerves, it was clarified that nerves in the retroperitoneum is little affected in animals whose pancreas was not fixed to the retroperitoneum whereas in animals with the fixation of the pancreas, degeneration or pathologic changes could be observed in the ganglion cells, nerves in the connective tissue around the abdominal aorta and those in the adventitia of the abdominal aorta. These findings are assumed to indicate infiltration of pancreatic exudate into the ganglion cells, the surroundings of the abdominal aorta and the adventitia of the abdominal aorta, eventually disturbing the regulation of blood pressure.

From the results of the present experiment, it is assumed that pathologic changes in the retroperitoneum at acute pancreatitis have important significance in occurrence of shock, particularly in lethal cases with fulminant course, and that these findings reveal some suggestions on surgical treatment of acute pancreatitis.

Accomplishing the present paper, the author is deeply indebted to Prof. Dr. Ichio Honjo for his valuable advices and kind encouragement throughout the experiment, and the author is also grateful to Dr. Hasebe and Dr. Miyazaki in our clinic for their kind helps.

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和文抄録

急性膵炎時の後腹腔病変の意義

京都大学外科第1講座（主任：本庄一夫教授）

中　川　俊　彦

犬の実験的膵炎において後腹腔病変の果す意義の解明に種々の実験を行なつた．

① 自家胆汁0.2cc/kg注入による膵炎犬は全例生存した．犬の膵を解剖学的に人の膵に類似せしめるため，膵頭上部を後腹膜に縫着したが全例生存し犬にさしたる影響は与えない．犬の膵後腹腔縫着を行ない，同量の自家胆汁注入により膵炎を起こさすと全例5～24時間後に死亡した．

② 自家胆汁0.4cc/kgを注入して得た膵炎犬では血圧は緩徐に下降し，門脈圧は上昇した．後腹腔縫着膵炎犬では血圧は急激に下降し，門脈圧も下降する．

③ Trypsin250mgを腹腔内に注入すると血圧は緩徐に下降し，門脈圧は上昇の傾向を示す．後腹腔へ注入すると血圧は前者に比し急激に下降し，門脈圧は下降する．

④ 後腹膜に小切開を加えておき，自家胆汁0.4cc/kg注入して得た後腹膜縫着膵炎犬では非切開群に比して圧変動は緩徐であり，死亡時間も延長する．同様に後腹膜切開の後，Trypsin250mgを後腹腔に注入すると，非切開群に比して血圧は緩徐に下降し，門脈圧は上昇する．

5) 非縫着膵炎犬，および後腹膜縫着膵炎犬の後腹腔に存在する神経組織についてBielschowsky氏鍍銀法—鈴木氏変法および巣鴨氏髄鞘染色法により神経組織学的観察を行なつた．

非縫着膵炎犬では後腹腔に存在する神経組織に対して何ら影響を与えず，縫着膵炎犬では節細胞，腹部大動脈周囲，腹部大動脈外膜に分布する神経に変性もしくは病的変化を認めた．これは膵滲出液が節細胞，腹部大動脈周囲，外膜へと浸潤したことを意味し，Stöhrの言う血圧調節に影響を与えたものと解される．

以上のことから急性膵炎時の後腹腔病変はショック，特に電撃的に死亡するものに対して重大な意義を有し，併せてその外科的治療に一つの示唆を与えるものと信ずる．

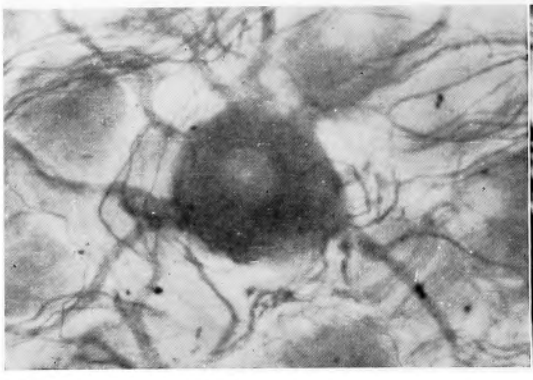

Photo 1 Ganglion Cells in Dogs with acute Pancreatitis and without Fixture of Pancreas. ×900
Bielschowsky Staining (Abbreviated to B-stain., hereafter)

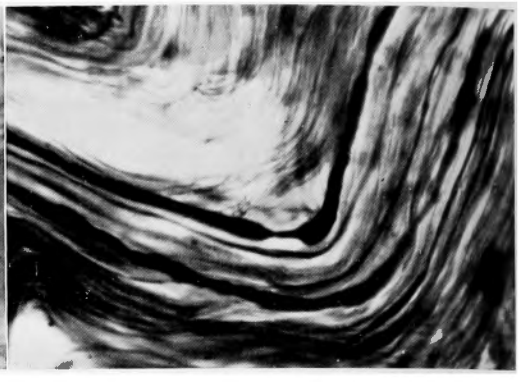

Photo 2 Nerves in Connective Tissue around Abdominal Aorta in Dogs with acute Pancreatitis and without Fixture of Pancreas. ×900
B-stain.

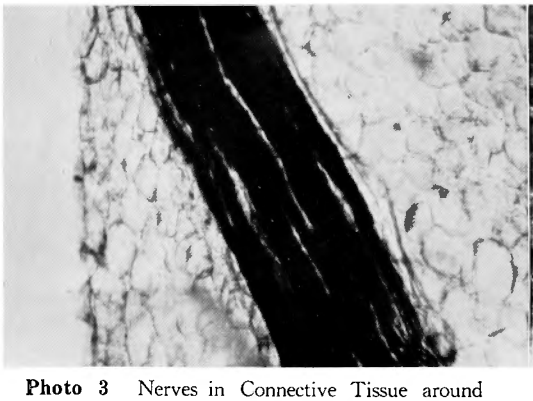

Photo 3 Nerves in Connective Tissue around Abdominal Aorta in Dogs with acute Pancreatitis and without Fixture of Pancreas. ×600
Myelin sheath staining of Sugamo's Method.

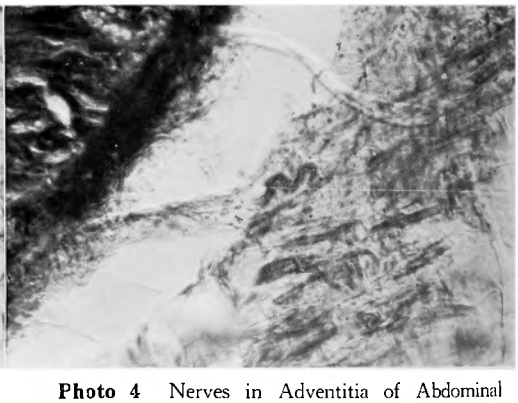

Photo 4 Nerves in Adventitia of Abdominal Aorta in Dogs with Pancreatitis without Fixture of Pancreas. ×600
B-Stain.

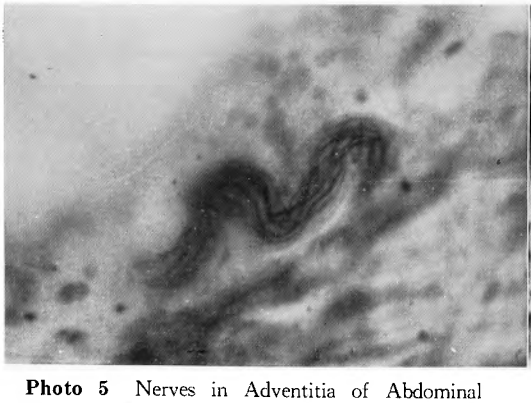

Photo 5 Nerves in Adventitia of Abdominal Aorta in Dogs with Pancreatitis without Fixture of Pancreas. ×900
B-Stain.

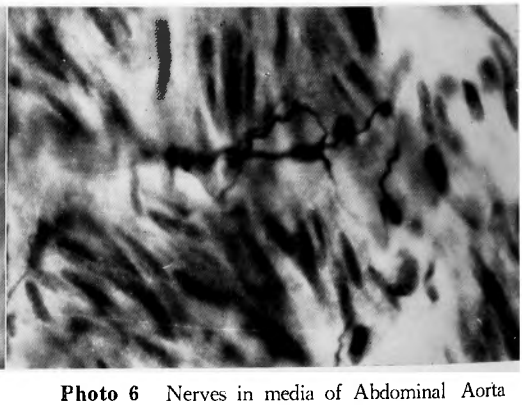

Photo 6 Nerves in media of Abdominal Aorta in Dogs with Pancreatitis without Fixture of Pancreas. ×900
B-Stain.

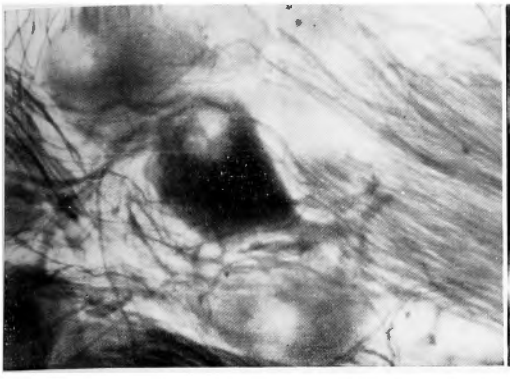

Photo 7 Ganglion Cells, Disappearance of Nuclei and Irregular Arrangement of Portars. Dog with acute Pancreatitis and with Fixture of Pancreas. ×900
B-Stain.

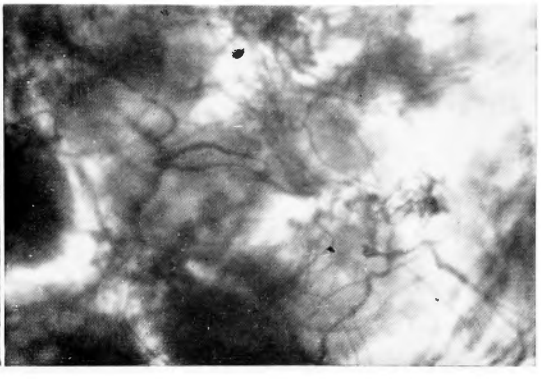

Photo 8 Ganglion Cells, Transposition of Nuclei Dog with acute Pancreatitis and with Fixture of Pancreas. ×900
B-Stain.

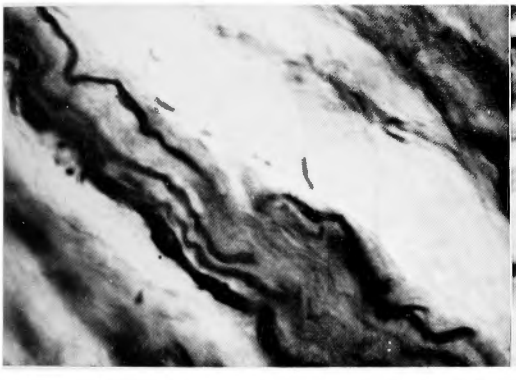

Photo 9 Nerves in Connective Tissue around Abdominal Aorta. Irregular Swelling, vacuole Formation. Dogs with acute Pancreatitis and with Fixture of Pancreas. ×900
B-Stain.

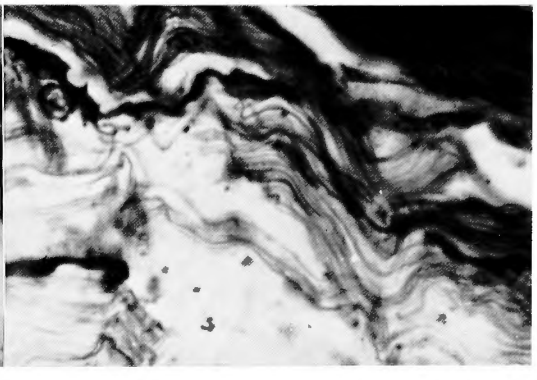

Photo 10 Nerves in Connective Tissue around Abdominal Aorta. Irregular swelling and tortuosity. Dogs with acute Pancreatitis and with Fixture of Pancreas. ×900
B-Stain.

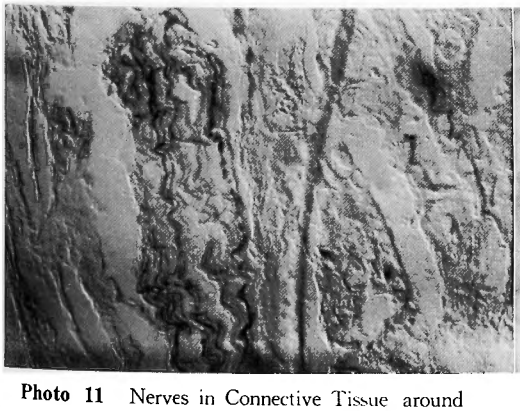

Photo 11 Nerves in Connective Tissue around Abdominal Aorta. Drop-like Fragmentation. Dogs with acute Pancreatitis and with Fixture of Pancreas. ×600
Myelin sheath staining of Sugamo's Method.

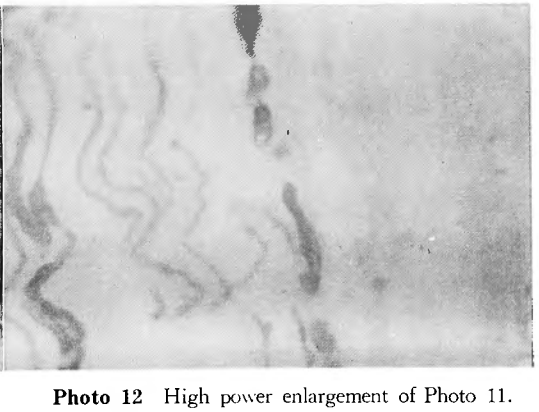

Photo 12 High power enlargement of Photo 11. ×900

Photo 13 Nerves in Connective Tissue around Abdominal Aorta. Drop-like Degeneration, Fragmentation, Irregular swelling. Dogs with acute Pancreatitis and with Fixture of Pancreas. ×600
B-Stain.

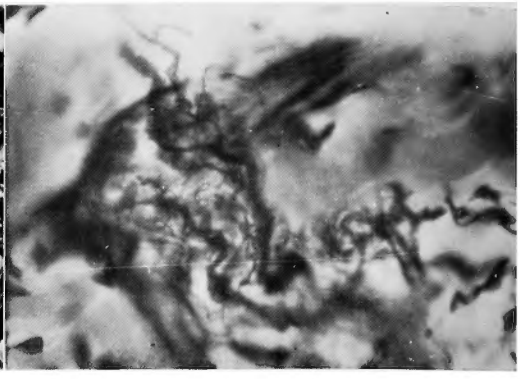

Photo 14 Nerves in Adventitia of Abdominal Aorta. Irregular tortuosity and swelling. Dogs with acute Pancreatitis and with Fixture of Pancreas. ×900
B-Stain.

Photo 15 Nerves in Adventitia of Abdominal Aorta. Irregular tortuosity and swelling. Dogs with acute Pancreatitis and with Fixture of Pancreas. ×600
B-Stain.

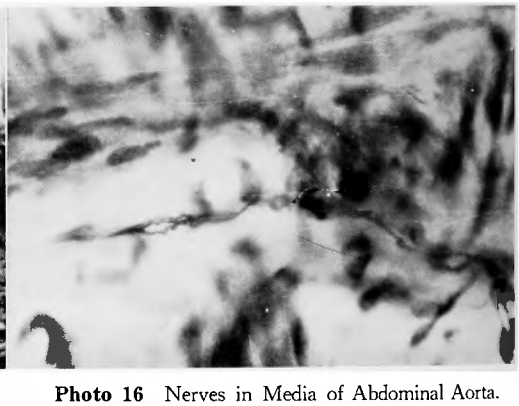

Photo 16 Nerves in Media of Abdominal Aorta. Dogs with acute Pancreatitis with Fixture of Pancreas. ×900
B-Stain.